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| EXAMINER |
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EPPERSON, JON D

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| ART UNIT | PAPER NUMBER |
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1639

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/629,984

Applicant(s)

SCHMIDT ET AL.

Examiner

Jon D. Epperson

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 5,6,9 and 11-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,7,8 and 10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on December 27, 2004.

Status of the Claims

2. Claims 1-16 are pending in the present application.
3. Applicant's response to the Restriction and/or Election of Species requirements is acknowledged (Applicant elected without traverse Group I, claims 1-10) and claims 11-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.
4. Please note: Applicant's elected species (Subgroup 2 = -COOH; Subgroup 3 = polystyrene solid support) was found in the art. Furthermore, Applicant's *specifically* elected species (Subgroup 1 = compound shown in figure 2b) was searched and was not found in the prior art. Thus, the search was expanded to non-elected species, which *were* found in the prior art, see rejections below. Also, see MPEP § 803.02 (emphasis added):

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. *The prior art search, however, will not be extended unnecessarily to cover all nonelected species.* Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that

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anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

5. Claims 5, 6 and 9 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species (see below i.e., *Response to Restriction and/or Election of Species*). Please note that the Examiner believes that claim 7 (and not claim 6) reads on the elected species because Applicants elected a “carboxylic acid” group (not an amino group) as the “reactive arm” group (e.g., see 12/27/04 Response, page 6, last full paragraph, “Applicant elects: ... (Subgroup 2) the species of carboxylic acid (-COOH) as the single species of reactive arm group”), which is found in claim 7, “... wherein said reactive arm group is a carboxyl group” and not in claim 6, “... wherein said reactive arm group is an amino group.”

6. Therefore, claims 1, 2, 3, 4, 7, 8 and 10 read on the elected species (e.g., see 12/27/04 Response, page 6, last two lines) and are examined on the merits in this action.

Response to Restriction and/or Election of Species

7. Applicant’s election of Group I (claims 1-10) **without traverse** is acknowledged.

8. Applicant’s election of species is also acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a) and/or 37 CFR 1.111(b)).

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9. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

10. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

11. The references listed on applicant's PTO-1449 form have been considered by the Examiner. A copy of the form is attached to this Office Action.

Specification

12. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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13. Claims 1-4, 7, 8 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the claimed invention (e.g., see *In re Edwards*, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978)). Applicants' claims are directed to a broad genus of compositions having a multifunctional chemical moiety covalently attached thereto at a resin attachment site, said multifunctional chemical moiety including hydrophobic anchoring groups thereon (e.g., see independent claims 1), which represents enormous scope because Applicants do not place any limitations on the number of atoms, types of atoms or the way in which said atoms can be connected together to form such a compound and/or composition. Thus, virtually an infinite number of possibilities would be included in Applicants' claimed scope encompassing virtually every known class and subclass of compounds (e.g., see also 35 U.S.C. 112, second paragraph "metes and bounds" rejection below). In addition, Applicants' more narrowly drawn sub-genera do not alleviate these deficiencies. For example, the specification does not define the term "derivative" as used in dependent claims 3 and 4. The specification and claims do not place any limit on the number of substitutions, deletions, insertions and/or additions that may be used to modify the amino acid structure to form said derivatives. Thus, the scope still includes an enormous number of structural variants.

In contrast, Applicants' specification provides only one working example of the claimed invention (e.g., see specification, pages 17-20; see also figures 2 and 5).

Applicants disclose the condensation of para-nitrophenyl carbonate Wang resin with a lysine multifunctional group containing a $(C_{18}H_{37})_2$ anchoring group (e.g., see Examples 1 and 2; see also figure 5). In addition, Applicants further disclose that the Wang immobilized lysine can be used in peptide synthesis to create peptides like "VPPYFTLMYGGGGK" (e.g., see Example 2).

Applicants are referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding adequate disclosure. For adequate disclosure, like enablement, requires representative examples, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention*. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. In addition, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05).

Here, Applicants have only provided one working example of the claimed invention (i.e., a polystyrene immobilized lysine that is used in peptide synthesis). Thus,

a person of skill in the art would not believe that Applicants were in possession of a genus that encompasses virtually an infinite number of compounds and/or compositions encompassing every class and subclass. For example, while solid phase synthesis of various compounds was known at the time of filing (i.e., resin containing compositions), such synthesis was not sufficiently routine or predictable at the time of filing, to permit one of skill in the art to devise strategies for the use of any solid support containing a multifunctional moiety having any active sites protected in any way. This type of synthesis requires high efficiency in the coupling steps and protection/deprotections and is further complicated by carryover, cross-reactions and/or unintentional cleavage, all of which are acknowledged issues in the art; each must be dealt with in the optimization of a solid phase synthesis scheme. A review article published by Janda in late 1994, discusses these issues (Janda, K. D. "Tagged versus untagged libraries: Methods for the generation and screening of combinatorial chemical libraries" *Proc. Natl. Acad. Sci.* **November 1994**, Vol. 91 pp. 10779-10785,. See especially page 10782-10785). Orthogonal protection of different reactive groups (active sites) was known in the art to be necessary for efficient solid phase synthesis (see Janda Figure 5, page 10783). The art of solid phase synthesis is known to be difficult to optimize, especially when multiple compounds are present (as discussed in Janda, set forth supra).

Furthermore, while Applicants have demonstrated that a para-nitrophenyl carbonate Wang resin can be used with the present invention, this would not allow a person of skill in the art to conclude that any resin could be employed. For example, Yan et al states, "A common problem in SPOS [solid phase organic synthesis] practice is that

reaction conditions can not simply be transferred from one kind of support to another. A set of reaction conditions may work well for polystyrene resins, but may fail completely for pin- or PS-PEG resin-based synthesis" (see Yan, B.; Gremlich, H. -U. "Role of Fourier Transform infrared spectroscopy in the rehearsal phase of combinatorial chemistry: a thin-layer chromatography equivalent for on-support monitoring of solid-phase organic synthesis" *J. Chromatogr. B: Biomed. Sci. Applic.* **1999**, 725, 91-102, especially page 97 paragraph 2).

Thus, applicants have not demonstrated in "full, clear, concise, and exact terms" that they are in possession of the claimed invention. The specification and claims do not provide any guidance as to what changes should be made to extend Applicants' one example to the infinite number of possibilities that are currently being claimed. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variable, Applicants' single example is insufficient to describe the enormous genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. *See Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993); *See also Brenner v. Manson*, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966) (noting, "A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

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14. Claims 1-4, 7, 8 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling compositions containing a “lysine” multifunctional group bound to a “polystyrene” resin that contains a membrane anchoring group with ~C₁₈ carbon chains, does not reasonably provide enablement for any multifunctional group bound to any resin containing any anchoring group. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. Some of these factors may include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims are drawn to a broad genus because Applicants do not place any limitations on the number of atoms, types of atoms or the way in which said atoms can be connected together to form such a composition. Thus, virtually an infinite number of possibilities would be included in Applicants’ claimed scope encompassing virtually every known class and subclass of

compounds (e.g., see also 35 U.S.C. 112, second paragraph “metes and bounds” rejection below). In addition, all of Applicants’ more narrowly drawn sub-genera are also not adequately described. For example, the specification does not define the term “derivative” as used in dependent claims 3 and 4. The specification and claims do not place any limit on the number of substitutions, deletions, insertions and/or additions that may be used to modify the amino acid structure to form said derivatives. Thus, the scope of even the more narrowly drawn subgenera still include an enormous number of structural variants. Consequently, the nature of the invention cannot be fully determined because the invention has not been defined with particularity.

(3 and 5) The state of the prior art and the level of predictability in the art: While solid phase synthesis of various compounds was known at the time of filing (i.e., resin containing compositions), such synthesis was not sufficiently routine or predictable at the time of filing, to permit one of skill in the art to devise strategies for the use of any solid support containing a multifunctional moiety having any active sites protected in any way. This type of synthesis requires high efficiency in the coupling steps and protection/deprotections and is further complicated by carryover, cross-reactions and/or unintentional cleavage, all of which are acknowledged issues in the art; each must be dealt with in the optimization of a solid phase synthesis scheme. A review article published by Janda in late 1994, discusses these issues (Janda, K. D. “Tagged versus untagged libraries: Methods for the generation and screening of combinatorial chemical libraries” *Proc. Natl. Acad. Sci.* **November 1994**, Vol. 91 pp. 10779-10785,. See especially page 10782-10785). Orthogonal protection of different reactive groups (active

sites) was known in the art to be necessary for efficient solid phase synthesis (see Janda Figure 5, page 10783). The art of solid phase synthesis is known to be difficult to optimize, especially when multiple compounds are present (as discussed in Janda, set forth supra).

Furthermore, while Applicants have demonstrated that a para-nitrophenyl carbonate Wang resin can be used with the present invention, this would not allow a person of skill in the art to conclude that any resin could be employed. For example, Yan et al states, "A common problem in SPOS [solid phase organic synthesis] practice is that reaction conditions can not simply be transferred from one kind of support to another. A set of reaction conditions may work well for polystyrene resins, but may fail completely for pin- or PS-PEG resin-based synthesis" (see Yan, B.; Gremlich, H. -U. "Role of Fourier Transform infrared spectroscopy in the rehearsal phase of combinatorial chemistry: a thin-layer chromatography equivalent for on-support monitoring of solid-phase organic synthesis" *J. Chromatogr. B: Biomed. Sci. Applic.* **1999**, 725, 91-102, especially page 97 paragraph 2).

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants' specification provides only one working example of the claimed invention (e.g., see specification, pages 17-20; see also figures 2 and 5). Applicants disclose the condensation of para-nitrophenyl carbonate Wang resin with a lysine multifunctional group containing a $(C_{18}H_{37})_2$ anchoring group (e.g., see Examples

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1 and 2; see also figure 5). In addition, Applicants further disclose that the Wang immobilized lysine can be used in peptide synthesis to create peptides like "VPPYFTLMYGGGGK" (e.g., see Example 2).

(8) The quantity of experimentation needed to make or use the invention base on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have not provided any working examples that would teach this enormous genus that falls within a highly unpredictable art area. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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15. Claims 1, 2, 3, 4, 7, 8 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claim 1**, the phrase “said multifunctional chemical moiety including hydrophobic anchoring groups” is vague and indefinite. For example, it is not clear whether the hydrophobic anchoring groups are part of the multifunctional group or are a separate entity apart from the multifunctional group? In addition, the claim does not provide a point of reference with regard to the “anchoring” function (e.g., are the hydrophobic groups anchoring to the solid support or some other chemical moiety; the claim does not state that it is a “membrane” anchoring group, which is defined in the specification as a hydrophobic group with 4-20 carbons that anchors to a membrane). Furthermore, Applicants’ species election indicates that the carboxylic acid group in core 105 of figure 2b is the “reactive arm group” (e.g., see 12/27/04 Response, page 6, last full paragraph, “... the carboxylic acid group in core 105 being the reactive arm group”). However, it is not clear how this CO₂H could be the reactive arm group when the claim further requires that said reactive arm group be attached “to said resin attachment site” because this CO₂H group is NOT attached to said resin attachment site, but rather to part of Applicants’ elected multifunctional chemical moiety instead (e.g., see figure 2b wherein the CO₂H is covalently linked to the CH group of the elected multifunctional group instead of the polystyrene resin). Consequently, the metes and bounds of the claimed invention cannot be determined. Therefore, claims 1 and all dependent claims are rejected under 35 U.S.C. § 112, second paragraph.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1, 2, 3, 4, 7, 8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al. (Singh, A.; Yao, Q.; Tong, L.; Still, W. C.; Sames, D. "Combinatorial approach to the development of fluorescent sensors for nanomolar aqueous copper" *Tetrahedron Letters* **2000**, *41*, 9601-9605).

For *claim 1*, Singh et al. (see entire document) disclose fluorescent sensors for aqueous copper ions (e.g., see Singh et al, abstract), which anticipate the claimed invention. For example, Singh et al. disclose a composition comprising a solid resid support (e.g., see page 9603, compound 8 wherein the circle indicates the resin support). Singh et al. also disclose a solid resin support having a multifunctional chemical moiety covalently attached thereto at a resin attachment site (e.g., see page 9603, compound 8 wherein the 1,4,7-triazonane could be considered the multifunctional chemical moiety i.e., each N constituted a different functional group or, in the alternative, the 1,4,7-triazonane (referred to herein as C₆N₃) chemically bonded to the ethylamine could be considered the multifunctional chemical moiety (i.e., the C₆N₃CH₂CH₂N portion of the molecule) or, in the alternative, the multifunctional chemical moiety could include the alkyl amide linkage (i.e., the C₆N₃CH₂CH₂N(CH₂)₅(C=O)-portion of the molecule or, in

the alternative, the multifunctional chemical moiety could be just the tri-functional $S(=O)_2-NCH_2CH_2N$ portion of the molecule. In addition, the multifunctional chemical moiety “includes” a hydrophobic anchoring groups (e.g., see page 9603, compound 8 wherein the hydrophobic $-(CH_2)_5-$ anchors the multifunctional group to the solid support or, in the alternative, the hydrophobic $-CH_2-CH_2-$ anchors the C_6N_3 to the solid support or, in the alternative, the $-CH_2-CH_2-$ anchors the multifunctional group to the C_6N_3 copper binding site, etc. Please note that there are many other variations that could read on Applicants’ claims (e.g., see also 35 U.S.C. § 112, second paragraph rejection above).

For *claim 2*, Singh et al. disclose a tri-functional moiety (e.g., see page 9603, compound 8 wherein the C_6N_3 represents the tri-functional moiety possessing three functional nitrogens or, in the alternative the $C_6N_3CH_2CH_2N$ represents the tri-functional moiety possessing two functional C_6N_3 nitrogens and one functional CH_2CH_2N or, in the alternative, the $NCH_2CH_2NS(=O)_2$ represents the tri-functional moiety possessing two functional nitrogens and one functional $(O=)S(=O)$ group or, in the alternative, the $S(=O)_2N(CH_2)_5C(=O)$ represents the tri-functional moiety containing an $S(=O)_2$ functional group, a N functional group and a carbonyl functional group. Please note that there are many other variations that could read on Applicants’ claims (e.g., see also 35 U.S.C. § 112, second paragraph rejection above).

For *claims 3-4 and 7-8*, Singh et al. disclose compound 9 wherein the $(O=)C-CH(CH_2CO_2H)-NH-$ portion of the multifunctional group represents an aspartic acid “derivative” that contains a carboxyl group that is covalently attached to said resin via the alkyl CH_2 linker.

For **claim 10**, Singh et al. disclose tentagel resin, which reads on crosslinked polystyrenes (e.g., see figure 1).

17. Claims 1, 2, 3, 4, 7, 8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Meienhofer et al. (Meienhofer, J.; Trzeciak, A. "Solid-Phase Synthesis with Attachment of Peptide to Resin through an Amino Acid Side Chain: [8-Lysine]-Vasopressin" *PNAS* **1971**, *68*, 5, 1006-1009).

For **claim 1**, Meienhofer et al. disclose an O-alkyl containing lysine epsilon coupled to a polystyrene gel (e.g., see Meienhofer et al., page 1006, compound 4), which anticipates the claimed invention. In this scenario, the solid resin is the standard Merrifield Resin (e.g., see page 1006, column 2, first full paragraph; see also compound 1) and the multifunctional chemical moiety is a lysine amino acid containing an R' O-alkyl hydrophobic anchoring group. Please note that the hydrophobic anchoring group could also be the t-butyl portion of the Boc group and/or the any of the hydrophobic portions of the vasopressin peptide (e.g., the phenylalanine, tyrosine side chains), which would allow it to "anchor" to its hormonal receptors in the cell membrane.

For **claim 2**, Meienhofer et al. disclose the trifunctional lysine wherein the ϵ -NH, α -NH and CO represent the three functional groups (e.g., see page 1006, compound 4).

For **claim 3-4**, Meienhofer et al. disclose a lysine amino acid derivative and a $(\text{CH}_2)_4$ - side chain and a reactive arm that contains a CO_2H or a $-\text{NH}_2$ after deprotection of the R' and Boc, groups respectively (e.g., see figure 4). The ϵ -NH might also be

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considered to be a reactive group (e.g., see 35 U.S.C. 112, second paragraph rejection, above).

For *claim 7*, Meienhofer et al. disclose both a reactive arm that contains a CO₂H or a -NH₂ after deprotection of the R' and Boc, groups respectively (e.g., see figure 4).

For *claim 8*, Meienhofer et al. disclose lysine (e.g., see figure 4).

For *claim 10*, Meienhofer et al. disclose Merrifield resin i.e., chloromethyl polystyrene-2% divinylbenzene (e.g., see page 1006, column 2, second full paragraph).

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
April 15, 2005

EXAMINER
JON D. EPPERSON
